

## POST-TYPHOID BONE LESIONS.

By HAROLD C. PARSONS, M.D.,

OF BALTIMORE,

ASSISTANT IN THE CLINIC OF PROFESSOR HALSTED IN THE JOHNS HOPKINS HOSPITAL.

AMONG the sequelæ of the continued fevers, the lesions of bone have long occupied a place of prominence. In the Toner Lecture, 1876, W. W. Keen quoted forty-one cases, thirty-seven of which had followed typhoid fever. He remarks that "typhoid as usual claims the larger share," inferring that such had been the experience of those before him. In the same year Sir James Paget described most fully, from the clinical standpoint, an inflammatory condition of bone occurring at various periods after typhoid fever, pursuing a more or less chronic course, with but little tendency to spontaneous recovery, except after long periods of time. He had observed some seventy cases, all after typhoid fever.

Prior to these observations, Murchison<sup>1</sup> reported necrosis of femur, tibia, and temporal bone following the same disease, and, later, Affleck described periostitis of humerus in two cases, and of the tibia in another.

Hayward<sup>2</sup> reported several cases, one of which did not go on to necrosis; also one of multiple lesion.

Jackson<sup>3</sup> observed periostitis of rib with necrosis occurring two months after typhoid fever, with recovery after seven months.

With the identification of the Eberth-Gaffky bacillus as the specific cause of typhoid fever, the nature of these bone lesions has been investigated more thoroughly, with results which have

<sup>1</sup> Continued Fevers of Great Britain, 1873, p. 582.

<sup>2</sup> British Medical Journal, Vol. I, 1885, p. 16.

<sup>3</sup> British Medical Journal, Vol. I, 1885, p. 428.

established a relation between them and the primary typhoid attack.

Ebermaier,<sup>1</sup> in 1887, obtained from two cases of suppurative post-typhoid periostitis the bacillus of Eberth in pure culture. Orloff,<sup>2</sup> in 1889, in a similar case of periosteal abscess, six months post-typhoid, found this bacillus alone. Achalme<sup>3</sup> cites a case of periosteal abscess of tibia, the pus of which showed only the typhoid bacillus; and Melchior<sup>4</sup> found this organism alone in a periosteal abscess of the tibia occurring ten and a half months after the attack. Golgi and others have had similar experience. In these cases the bacillus of Eberth was regarded as the sole infective agent.

At about the same time Pean and Cornil<sup>5</sup> reported a case of necrosis of the tibia, occurring eight months after recovery from typhoid fever, examination of which showed the typhoid bacillus associated with other organisms.

Fashing<sup>6</sup> reported a somewhat similar case, in which staphylococci alone were found.

E. Fraenkel<sup>7</sup> found pyogenic organisms associated with the typhoid bacillus. He does not think that the typhoid bacillus plays an important *rôle*, but holds that the condition is one of secondary infection by the pyogenic cocci, and where these have not been found they have died out or the culture medium has not been suitable.

From time to time a large number of cases have been observed, varying more or less in the character of the infection. Thus, Achalme, Melchior (as above stated), Sultan, Chantamesse, Widal, and others, have reported cases of pure typhoid infection. Klemm speaks of a mixed infection, with the colon and typhoid bacilli; and one of our own cases showed the typhoid bacillus associated with the staphylococcus pyogenes citreus.

<sup>1</sup> Deutsches Archiv für klin. Med., Bd. XLIV, p. 141.

<sup>2</sup> Centralbl. für Chirurg., May 24, 1889.

<sup>3</sup> La Semaine Médicale, 1890, T. x, p. 224.

<sup>4</sup> La Semaine Médicale, 1892, T. XII, p. 304.

<sup>5</sup> Bull. de l'Académ. de Méd., 1891, No. 15.

<sup>6</sup> Wiener klinische Wochenschrift, 1892, No. 18.

<sup>7</sup> Baumgarten's Jahresbericht, VI, p. 225.

There are many cases on record in which the infection has not been with the typhoid bacillus, but with the pyogenic cocci, or the less frequent pus producers. Netter describes eleven cases of osteitis, five of which showed the pneumococcus, one the pneumococcus and staphylococcus, and five the streptococcus.

While it is certain that mixed infections do occur in these post-typhoid bone lesions, it must be admitted that the evidence of careful bacteriological investigation, based upon a considerable number of cases, is to the effect that these lesions may be caused by the typhoid bacillus alone.

The question of the pyogenic properties of the typhoid bacillus is of great interest in connection with these sequelæ of the fever.

Orloff produced suppuration in dogs and rabbits by subcutaneous inoculation of pure typhoid cultures, the pus showing this organism alone. Adenot,<sup>1</sup> by similar inoculation, caused pus formation in the subcutaneous tissue of dogs and rabbits, the typhoid bacillus was separated in pure culture.

Of greater interest, in the consideration of bone lesions, are the experiments of Golgi, who fractured a long bone in one of the lower animals, and at some distance from that point injected subcutaneously a suspension of pure typhoid bacilli, with the production of suppuration at the point of fracture; the pus showing in culture only the typhoid bacilli.

The presence of the typhoid bacillus in the spleen and bone-marrow, particularly of the ribs, has been demonstrated by Quinke as late as the seventh week of the disease. In nine cases examined, eight showed the organism in the marrow of the ribs. In two cases the sternum was examined with positive results, and in seven out of eight cases large numbers were found in the spleen pulp. By analogy they should be as frequent in the bone-marrow as in the spleen. The autopsy records of the Johns Hopkins Hospital show many instances in which typhoid bacilli have been found in the different organs of the body, in the bone-marrow and bile.<sup>2</sup> Dr. Welch has observed their persist-

<sup>1</sup> *Archiv de Méd. expérimentale*, T. I.

<sup>2</sup> Flexner, *Journal of Pathology and Bacteriology*, April, 1895.

ence in the bile of a rabbit which had been inoculated four months previously and had recovered ; they were not found in the organs. As showing the tenacity of life of the organism, Schiller implanted the bacilli on a silk thread, and at the end of one year they were found still living. According to the same author they can exist on a potato culture for two years.

Uffelmann found the bacilli alive in dry sterile sand at the end of eighty-two days.

These points throw some light upon the occurrence of post-typhoid bone lesions at periods long after the primary attack, which, as will be seen later, is one of the striking clinical features. It is, moreover, on these grounds that the theory of mixed infection is based,—that the entrance of pus cocci upon a soil already vitiated by the presence of the typhoid bacillus determines the suppuration, the pus organisms later dying out and leaving the bacilli alone in the focus, but it is an open question as to whether or not this really does occur. The experiments of Klemm have a very significant bearing upon this point. Into the ear vein of a rabbit he inoculated a pure culture of typhoid bacilli, and seven days later, in the same animals, and in the same manner, inoculated a pure culture of staphylococcus pyogenes aureus, with the result that an osteomyelitis—with, in one case, separation of the epiphysis—was set up, cultures from which showed the staphylococcus pyogenes aureus alone. Again, by the inoculation of both organisms together he produced an osteomyelitis of the ilium, cultures from which also showed staphylococcus pyogenes aureus alone.

The problem of the etiology of the post-typhoid bone suppurations appears to be twofold. Observations upon suppurative processes in human beings, developed during or subsequent to an attack of typhoid fever, indicate that at one time the ordinary pyogenic organisms are alone present, at another, associated with the typhoid bacillus, and in still others the typhoid bacilli alone are met with, and even more rarely the typhoid bacilli are found together with other bacteria,—*e.g.*, bacterium coli commune. It is not necessary that there shall be a common etiology in these processes any more than we look for

a common cause of suppurative processes occurring under other conditions in the body; on the other hand, there seems to be no good reason for excluding the typhoid bacillus from the group of possible pyogenic micro-organisms. It may be looked upon as capable of causing various pathological conditions,—a specific typhoid fever attack, a local suppuration, and, finally, a general septicæmia, as in a case which recently occurred in this hospital and was reported by Dr. Flexner.<sup>1</sup> The pyogenic organisms are often present in the intestine, and it is not surprising that they should also, at times, penetrate the interior when a ready means of entrance is afforded by the open ulcers present.

During the past year six cases of post-typhoid bone necrosis have come under our notice. Four were admitted to Dr. Halsted's service in this hospital, to whom I am indebted for the privilege of reporting them. The other two we were able to study in private practice through the kindness of Dr. Osler and Dr. Finney.

CASE I.—A. T., aged thirty-five years, cigar-box maker, admitted to Ward E, March 19, 1894, with a discharging sinus over left costal margin. The family history was negative. Inquiry into the previous history revealed no serious illnesses. There was no history of venereal infection. He had typhoid fever in August, 1893, the attack lasting three months. During convalescence, and while still in bed, patient suffered from what he describes as constant sticking pains over left costal margin, more or less severe, to which the attention of the physician in attendance was frequently called.

In November—*i.e.*, one month after recovery from attack, the pains however persisting,—there appeared an inflammatory area over the left costal margin, high up towards the xiphoid cartilage. There was no cough, no dyspnoea.

In December an incision was made into the tumor, blood escaping (according to the patient's description), after poulticing for some time a purulent discharge appeared, which has persisted.

On admission the general condition was good. Examination of the thoracic and abdominal organs was negative. There were no glandular enlargements; the note on condition of chest-wall is as follows:

<sup>1</sup> Journal of Pathology and Bacteriology, April, 1895.

Midway between xiphoid cartilage and the left nipple is a bright-red inflamed area, two by two centimetres, and in the centre of this the opening of a sinus. A probe passes three centimetres into the sinus backward and downward to the cartilage of the seventh rib. Around this inflammatory area the tissues are denser than normal and slightly painful to the extent of ten centimetres from above downward, and eight centimetres laterally. Highest temperature record 99.5° F. Urine was negative : no diazo reaction.

Operation March 22, 1894. Dr. Bloodgood. The granulation tissue was found behind the seventh costal cartilage, which was perforated. Posterior periosteum was not incised, but curetted. All diseased soft parts removed. The wound was irrigated and loosely closed. The cartilage was perforated in three places from cavity to sinus.

By March 26 some of the stitches were removed. Wound in central part gaping ; slight bloody discharge. The wound showed little tendency to granulate.

April 2. Patient was discharged. The sinus was still present, discharging a brownish pus.

April 6. Patient returned for dressing. A swelling was noticed over the left costal margin below wound of former operation. Healthy tissue separates the two. There is pain in the swelling and in lower part of back on same side.

April 12. Patient readmitted to hospital. Wound of former operation looking well, granulating from bottom well ; sinus still discharging ; swelling over costal margin below is as at last note, but more painful. There is no redness, no oedema ; severe pain in back and left side low down.

April 15. A friction murmur was heard just above the swelling ; fluctuation was evident in tumor ; pain was not so severe as at time of last note.

April 19. Pain in swelling much greater ; fluctuation more marked ; friction murmur no longer heard.

April 19. Operation : Dr. Finney. Excision of old sinus and some cartilages ; opening of abscess over costal margin ; much thick greenish-yellow pus evacuated ; wound irrigated (1 to 1000) hydrarg. bichlor. solution ; packed with iodoform gauze. Shortly after operation the patient left the hospital, returning every few days for dressing.

May 11. Wound granulating rapidly ; no cartilages exposed.

May 29. Wound healed except at two points : all pain has left the back for the last two weeks.

August 1. There is a small sinus discharging very little pus in centre of last wound ; general health is much improved : the cultures at this time showed the typhoid bacillus and staphylococcus aureus.

December 14, 1894. Wound perfectly healed, scar depressed, and it looks healthy ; there is no pain ; scar runs parallel with left costal margin, five centimetres above it ; patient says wound has been completely healed since August 15 ; the only symptom is a feeling of numbness along costal margin corresponding to the scar.

*Bacteriological Report.*—March 22, 1894. Culture at operation, agar slant made ; the pus was noted as being thick and gelatinous, and a general necrotic condition existed about the focus ; twenty-four hour growth plated.

March 23. Petri plates of yesterday show large and small grayish colonies. Under low power, large colonies,—circular and oval, granular generally, with darker circumscribed centres, in the paler periphery darker spots are seen like the centre, but smaller. Cover-slips from both large and small colonies showed short bacilli with rounded ends, growing often in pairs, which stained faintly ; also longer bacilli forming long threads.

Agar slant from colony, in twenty-four hours, shows uniform grayish growth along smear ; after several days, fringe-like growth from edges ; sour smell.

Gelatin rolls: Whitish or grayish colonies spread out on surface, and small, darker, deep colonies. The superficial colonies had dark yellowish centres, the periphery being much paler and of a gray color ; the edges were uneven and wavy ; no liquefaction of the gelatin.

Low power: In places a double fringe is noted at the edge ; the markings in outer part are mostly parallel with border, or nearly so.

Bouillon: Clouding in upper zone,—Potato: No growth perceptible. Cover-slip showed the same organisms as the above.

Litmus milk showed faint reddening ; no coagulation.

Lactose agar, 1 per cent. : No fermentation, though abundant growth along the stab.

Indol reaction: With and without nitrite, negative ; parallel culture of colon positive. Hanging drop preparation showed the organisms very motile. Plated with Hg: marked double zone about Hg. The appearance of the cultures was unchanged after many days.

About one month after first operation, cultures from the sinus showed typhoid bacillus in pure cultures.

<sup>1</sup> Bolton, International Medical Magazine, December, 1894.

Fourteen weeks after second operation cultures from sinus showed typhoid bacillus and staphylococcus pyogenes aureus.

Conclusion: Typhoid bacillus.

CASE II.—S. M., female; married; aged forty-three years; admitted to hospital April 2, 1894.

There is a definite tuberculous history. Diseases of childhood; scarlet fever; one miscarriage (at second month); pneumonia ten or twelve years ago; patient has expectorated blood several times during last winter, at times bright red, and at times mixed with sputum; two ounces was the largest quantity at any time.

Typhoid fever in September, 1892; was up and about in following November.

In January, 1893, she began to have pain in right side over lower ribs, and noticed that the soft parts over painful area were more prominent than on left side. Pain over lower ribs on coughing and on drawing a long breath; this pain over lower ribs became less, but never entirely disappeared. Six weeks ago noticed soreness over seventh, eighth, and ninth costal cartilages on right side; a few days later noticed that the skin was purplish in color, and that there was a hard swelling over the seat of pain. This swelling became very painful and gradually larger. Poultrices have been applied, and a small projection has formed on its surface.

At present, general health good; local condition as described above; the swelling was incised in the ward, and cultures were taken; urine negative; no diazo reaction.

April 6. Operation: Dr. Finney. Excision of sinus and costal cartilages of seventh and eighth ribs. The sinus leading downward and outward begins to the right of the ensiform, extending to the cartilage of the seventh rib, which is perforated. Other sinuses were formed behind this, and between it and the sixth, and between it and the eighth. These sinuses were lined by soft, reddish granulation tissue; the perichondrium was thickened; cartilages and sinuses were excised; some cartilage was left in the wound; iodoform gauze packing after irrigation with (1 to 1000) hydrarg. bichlor. solution.

April 9. Wound granulating, except over cartilages in floor of wound; temperature 104° F.

April 18. Granulations healthy, except over exposed cartilage. Temperature 99° F. on April 12, to-day temperature is normal.

May 30. Patient was discharged. Sinus still discharging. Patient to return for dressing.



June 13. All healed except over small point of exposed cartilage. Some pain over ribs under angle of scapula.

June 23. Sinus curetted. Bacilli and micrococci found in cover-slips of discharge.

June 26. Patient was readmitted for further operation.

June 28. Operation: Dr. Bloodgood. Three cartilages found involved. They were excised as far as costal junction from sternum, at which points the periosteum was not thickened, and cartilages appeared quite normal. At all other places the periosteum was adherent and thickened, sinuses filled with granulation tissue, and the cartilage was riddled with small sinuses. Highest temperature since discharge was 102° F.

July 3. First dressing; doing well.

December 20. All healed except small area, more an excoriation than granulating area, slight dermatitis about it. Breast is pendulous and hangs over wound. There is no sinus. General condition is good. Wound has been healed about two weeks.

*Bacteriological Report.*—Cover-slips. Agar slants were made from pus obtained when mass was first incised.

Cover-slips: Bacilli varying in length from two times to several times as long as broad.

Agar slant (forty-eight hours): Whitish growth along line of smear and stab; tendency to run out from stab by sort of fringe. Growth plated.

Petri plates: Slow colonies as in Case I. Only one variety of organisms. Isolated.

Gelatin slant (forty-eight hours): Grayish-white raised colonies; glistening surface; outline wavy. Centre more opaque than periphery; colonies quite discrete; shapes vary; no liquefaction of gelatin.

Cover-slips show bacilli, mostly short with rounded ends; some straight, others slightly curved; also very long bacilli; segments not well marked.

Gelatin rolls: Seven days old. Grayish-white colonies spreading out on surface; centre more opaque than periphery; edges uneven and wavy; no liquefaction.

Low power: Central mass brownish and granular; periphery paler, gray; darker markings, mostly linear; margins uneven and wavy.

Litmus milk: Very faint reddening; no coagulation.

Potato: No visible growth (cover-slip showed organisms).

Lactose agar: No fermentation; abundant growth.

Indol reaction: With and without nitrite, negative; parallel cultures of colon, positive.

Motility: Actively motile; the field shows short, very motile bacilli; also long threads traversing the field with wavy motion.

Plate with Hg: Double ring and sterile zone; zone about seven millimetres wide.

Six weeks after first operation cultures from sinus showed typhoid bacilli and staphylococcus pyogenes aureus. Most of the primary tests were repeated for confirmation.

Conclusion: Typhoid bacillus.

CASE III.—J. K. (hospital No. 10,792), male, aged thirty-six years; married; German; tailor; admitted to hospital September 5, 1894, complaining of painful swelling over right tibia, and discharging sinus over left tibial crest.

Family history unimportant. Previous history: no serious illnesses with exception of typhoid fever in October, 1893. No history of venereal infection. Habits: smokes and drinks moderately. The patient was taken ill with typhoid fever on October 4, 1893, was in bed four weeks, and for two weeks was very delirious; early in November patient was up and about. During the three weeks after rising from bed the patient experienced vague pains first in right arm and forearm for a few days, then in left leg, then over right costal margin, these were slight and soon passed off.

On November 26 there was more acute pain over *left tibial crest*, increasing in severity, and later redness and swelling. Early in December incision was made into the swelling with instant relief. About the middle of December incision was necessary in another spot above the first, and on February 1 another incision was made below the others, when a splinter of bone was removed. The sinus is still discharging. There was no pain after first operation. Patient was able to work until time of admission to hospital.

Right Leg. In November, 1893, a slight pain was noticed in the right leg over tibial crest, and a small hard nodule the size of a small nut was found. The pain was always present, but very slight. There was no history of trauma. This remained so from November, 1893, to September 1, 1894, when the nodule became red and painful, and on September 5 the patient was admitted to hospital.

At present, general condition good; thoracic and abdominal organs negative; temperature has not been higher than 99.5° F. since admission; urine negative.

Right Tibia. The middle third is occupied by a fusiform enlargement, twelve centimetres long by five centimetres wide. This area is remarkably reddened and brawny, and the skin is cedematous. Over the most prominent point fluctuation is distinct, the area of fluctuation being definitely outlined. The entire involved area is very tender; there is constant pain, more or less severe.

Left Tibia. About middle of crest is a small sinus opening, five by five millimetres, surrounded by dense inflammatory tissue. There is slight purulent discharge from sinus; probe passes two centimetres down to bone.

September 6. On the day following admission the right leg was prepared as for operation, and with all possible care the fluctuating mass was aspirated for bacteriological purposes; about ten cubic centimetres of a brownish-red fluid was withdrawn; this was of a very gelatinous consistence, and was odorless; this was plated immediately.

September 7. The condition of right tibia has almost completely subsided; redness and swelling with pain are much less marked.

Operation: Dr. Werckmeister. Right tibia shows periosteal abscess containing brownish-red gelatinous exudate. This was completely excised; bone beneath found not involved; wound packed with gauze.

Left Tibia. On stripping back periosteum from front of tibia, two new bone sinuses are found and the surface of the bone rough; this was chiselled away and further sinuses with soft bone granulations and pus were found. All the anterior part of bone was removed, and back near posterior wall a sequestrum, one centimetre by one millimetre, was found; the operation was very extensive; only the posterior wall of the bone was left; the diseased skin excised. Pure carbolic acid was applied and irrigation  $\frac{1}{1000}$  HgCl<sub>2</sub>; gauze packings were used; secondary sutures were passed.

September 10. Left leg doing well; secondary suture tied; right leg also doing well.

September 16. Left leg is doing well; slight sero-purulent discharge; general condition good.

*Bacteriological Report.*—September 6. Right tibia. Fluctuating mass aspirated; grayish-brown pus, very gelatinous and sticky, apparently no curds nor shreds in it; it contains some blood.

Petri plates, agar slants, and cover-slips were made at once.

Cover-slips negative; although many leucocytes and red blood-corpuscles were present.

Plates (twenty-four hours): Colonies were: superficial (I) and deep (II). Colony I: About five millimetres in diameter, slightly raised, centre small, dense, and white; periphery grayish, also rather dense, edge regular, surface glossy.

Cover-slip: Short segmenting bacillus with larger forms; agar slant made; other colonies are paler, but the organisms were apparently similar. Colony II shows same organisms as No. 1.

September 8. Colony I: Agar slant (twenty-four hours): Grayish, pearl-like growth along line of smear; a fringe-like unevenness along edge.

Gelatin stab (six days old): Free growth along stab of small white colonies; no liquefaction.

Bouillon (twenty-four hours): Slight cloudiness, granular sediment.

Litmus milk (twenty-four hours): Faint reddening, no coagulation.

Potato (twenty-four hours): No visible growth.

Lactose agar (twenty-four hours): Faint growth along stab; no fermentation.

Hanging-drop preparation showed organisms very motile as short rods; also long chains of larger organisms were seen having a wavy motion across the field.

Indol reaction ( $\text{H}_2\text{SO}_4$ ) with and without nitrite, negative.

Cultures (after ten days): Still no visible growth on potato; no fermentation; no coagulation of milk, only faint pinking; no color to agar cultures.

Conclusion: Typhoid bacillus.

CASE IV.—H. H., male, aged twenty-nine years; traveller; admitted to hospital December 1, 1894, complaining of inflammatory condition over crest of right tibia. Family history negative. Personal history: *Childhood*, measles, mumps. *Adult life*, vague history of malaria. Venereal history: gonorrhœa six years ago, four and a half years, and three years ago; recovery apparently complete. Habits: alcohol in moderation; smokes but does not chew tobacco. Patient was in Ward C from October 8 to November 2 with typhoid fever; had been ailing about ten days (three days in bed) previous to admission.

*Present Illness*.—While still in bed during convalescence from

typhoid fever there was pain in right foot and discharge of small amount of pus from just below right fifth toe. At the same time there was also considerable pain over right tibial crest, markedly worse from 5 to 12 P.M.

After leaving hospital pain became much less severe, almost unnoticeable. From November 8 to 24 only occasional very slight pain.

From November 24 gradual increase of pain, worse at night; no history of any trauma, but patient had been almost constantly on his feet. On November 26, a swelling appeared over crest of right tibia; no reddening of surface. There was increase of pain until November 28.

On November 29, an incision was made into the mass; no pus escaped, only blood, giving immediate relief from pain.

Patient was admitted to hospital December 2, 1894. General condition good; thoracic and abdominal organs negative. Urine, 1035, acid, sweetish odor. Chemically: phosphates; no albumen; no sugar; no diazo. Microscopically negative. Over right tibial crest is a uniform enlargement seven centimetres from above downward, in the centre of which is an opening three centimetres long, slightly gaping, the seat of former incision. There is no pain, but the part is very tender. There is no rise in temperature. Patient feels well. No bare bone is felt in wound; wound is filled with blood-clot.

December 4, 1894. Operation: Dr. Halsted. A thin layer of bone was chiselled away. Excision of diseased tissues; wound closed with silver skin stitches after thorough irrigation with hydrarg. bichlor. (1 to 1000).

December 13. First dressing; doing well; cultures taken.

December 21. Patient was discharged; wound almost healed; slight granulation along incision.

March 17, 1895. Wound entirely healed; no pain.

*Bacteriological Report.*—Operation, December 4, 1894. The pus was of grayish-yellow color, thick, but not tenacious; no odor. Granulations necrotic, surrounding tissues, especially muscle, markedly necrotic, and of translucent, hyaline appearance. Bouillon and agar slant cultures made at time of operation; also cover-slips of pus.

Cover-slips negative as regards organisms.

Three hours after the first cultures were taken Petri plates made from bouillon cultures and from pus that had been put on the agar slant.

December 7, 1894. Agar slants and plates. Discrete grayish colonies, irregular outline, pearly lustre, slightly raised.

Cover-slips: Show short, moderately thick bacilli; length, two or three times the breadth; ends rounded, also larger forms in shape of longer and somewhat thicker bacilli; no threads were seen. Agar slant made from a discrete colony. Agar slant (forty-eight hours): Shows pearly growth along smear.

Gelatin stab (three days): Free growth along stab; no liquefaction.

Inoculations upon potato (twenty-four hours) showed no visible growth. (Organisms in cover-slips.) Litmus milk (twenty-four hours): very faint pinking, no coagulation. Dunham's solution (twenty-four hours): clouding. Glucose agar (1 per cent., twenty-four hours): distinct growth along stab; no fermentation. The organism is very motile; in the field it is seen as short, single bacilli (very motile), and larger, longer forms (less motile).

Indol reaction (the culture having been in Dunham's solution), with and without nitrite, proved negative. Petri plate with Hg gives wide sterile zone and a double fine ring.

January 4, 1895. The appearance of the cultures of December 9, 1894 is still unchanged.

Conclusion: Typhoid bacillus.

Tissues removed at operation: Dr. Bloodgood. The sinus over the tibia is 3.5 centimetres by seven millimetres, removed with a margin of skin from .5 to 1 centimetre wide. The sinus leads to a cavity at the bottom of which is the thickened periosteum, beneath which there has been a formation of new periosteal bone, easily stripped from the surface of the old shaft in thin laminæ. The bone itself shows no marked pathological changes. The periosteum is thickened from three to four millimetres, is grayish in color, and opaque. The granulation tissue of the cavity is grayish and glistening, dotted with fine pin-point red spots, and does not differ from that seen in a syphilitic periostitis, but the tissue about this cavity shows marked changes not noted in syphilitic periostitis.

The aponeurosis of the muscle is thickened and more opaque in color. The muscle has lost its bright red color and is gray. One sees in this tissue beneath the skin and parallel to it alternate white and red streaks.

CASE V.—Miss T., aged twenty-one years, was brought to Dr. Osler on November 23, 1894, by Dr. Bishop, complaining of general debility and a sore leg.

She has never been a strong girl, had always had poor digestion, and throughout the summer of this year was not at all well. In August she had an attack of fever, which began with headache and vomiting. She was extremely weak, and Dr. Bishop suspected typhoid fever. After persisting for a couple of weeks the fever subsided, but in ten days there was a slight return. The doctor remained uncertain about its nature, as she never had diarrhœa or any abdominal symptoms. Early in October she began to have great pain about the middle of the right tibia, and also on the front of the left forearm. Swelling soon followed in both regions, and on the leg a phlegmon developed, with much redness and swelling. This was lanced about a week ago by Dr. Bishop, and discharged a quantity of pus. The inflammation at the middle of the right arm gradually subsided.

*Present Condition.*—She is healthy looking, complexion not very good, owing to the presence of numerous pimples. The tongue is a little furred. The pulse is good, and there is no fever. The right leg is very much swollen from the ankle to the knee. In the middle of the anterior surface there is a large area of redness over which the skin is glossy, and an incision about two centimetres in length, from which a thin, sanious pus exudes. There is pitting above the ankle and a good deal of tenderness in the leg, but she is able to walk upon it.

On the left arm about the middle of the shaft of the radius there is a swelling about three by two centimetres, which projects quite prominently. The skin is not reddened and not adherent. It feels firm and is very sensitive to the touch. The patient was transferred to the care of Dr. Finney.

November 30, 1894. Operation: Dr. Finney. Left radius. Over lower end on ulnar side was a slight elevation, very painful; no redness over surface. Incision in long axis of arm, four centimetres in length, down to periosteum of radius, which was found thickened and adherent to bone beneath. This was turned back and exposed a bone of spongy consistence. This was incised; and pus of a grayish color and thick consistence was found and removed. A distinct cavity was found in the bone, containing a small sequestrum ten by two millimetres. The cavity was curetted and iodoform gauze packing inserted. The skin wound was partially closed about the packing. Cultures were taken; much pus was placed upon an agar slant.

Right Tibia. Over crest of tibia about the middle was an incised wound about three centimetres long, discharging a brownish pus, the

seat of former operation. Above this the skin is much discolored and of purplish color and very thin; there is distinct fluctuation.

November 30, 1894. Operation: Dr. Finney. The old wound was excised, and the excision was extended up through fluctuating point above; a dark, brownish colored pus of viscid consistence was evacuated. The skin was much undermined, and a regular phlegmonous condition existed. Cavity and pockets were well curetted and packed with iodoform gauze, after irrigation with hydrarg. bichlor. solution (1 to 1000).

*Bacteriological Report.*—Left Radius: Osteomyelitis; with sequestrum formation.

Right Tibia: Periostitis with phlegmon above seat of lesion subcutaneously.

November 30, 1894. Petri plates and slants were made from the pus twenty hours after operation. Cover-slips made from the pus were negative.

The original agar slants show discrete colonies after twenty-four hours. From radius colony I shows colonies of irregular outline, grayish, pearly surface, slightly raised. With transmitted light there is a distinct pearly lustre; the centre is more opaque and more yellowish than the periphery. Cover-slips show short, thick bacilli with rounded ends, also larger forms. Colony II is round, with regular outline, raised surface, shiny; the difference between centre and periphery is not very marked, the latter being slightly paler and thinner. Cover-slip shows a coccus,—singly, in pairs, and in groups.

Colony I.—Agar slant (five days old): Uniform grayish film over surface (the agar is very moist). Cover-slip as above.

Gelatin stab (two days): distinct growth; no liquefaction. Potato (four days): no visible growth; organism on cover-slip. Litmus milk (four days): faint pinking; no coagulation.

Organism was found very motile. Dunham's solution (two days): faint clouding. Indol reaction: With and without nitrite, negative.

Glucose agar (two days): distinct growth along stab; no fermentation.

In some cases there was a yellowish filmy growth on potato, likely due to some peculiarity in the medium, as other cultures gave an invisible growth.

All these cultural tests were repeated later, giving the same results as above, excluding the visible growth upon potato.



Colony II.—Agar slant (five days): General growth of small pin-head colonies, now assuming a yellowish color.

Gelatin (several days): distinct growth along stab; slight liquefaction of nearly half the gelatin. Potato (seven days): distinct lemon-yellow growth. Litmus milk: faint pinking; no coagulation; no further change at end of six weeks.

Dunham's solution (seven days): slight clouding.

Glucose agar (seven days): distinct growth; no fermentation.

Right tibia: The pus was of brownish-red color, was odorless, thick, and gelatinous.

After five days the original agar slant showed discrete colonies, whitish or yellowish in color, having circular, regular outlines; surface being raised.

The cover-slip showed a small coccus, in pairs, groups, and chains of four to eight.

Agar slant (two days): Shiny, pearly growth, regular margins, slightly raised.

Gelatin stab (two days): growth along stab; slight liquefaction. Potato (one day): dry, raised, golden-yellow growth. Litmus milk (one day): no change as yet. Dunham's solution (one day): slight clouding. Glucose agar: yellowish growth along stab; no fermentation.

Twenty days later. Potato: rich golden-red growth, raised and dry. Litmus milk: decided reddening; no coagulation. Gelatin: marked liquefaction.

At the end of seven weeks. Potato: as above. Litmus milk: a solid yellowish coagulum. Gelatin stab: four-fifths of medium liquefied.

Conclusion: *Staphylococcus pyogenes aureus* in the right tibia; in the left radius the *bacillus typhoideus* and the *staphylococcus pyogenes citreus*.

CASE VI.—Dr. (?) had typhoid fever from March 8 to April 25, 1894. During the past two months he has been at work. While still in bed he noticed a twinge of pain just above the left costal margin; it has increased and extended along the eighth rib; there is now on this rib, from mid-axilla to nipple line following the course of the rib, a definite swelling, which causes slight projection of the skin, which, however, is freely movable and uninvolved; there is no fluctuation, no special soreness, except on deep pressure.

His general condition is excellent; he looks well; tongue is

clean; percussion is clear over the axillary and lower mammary regions; no pleural friction; a few small crackling, probably pleural râles on deep inspiration over mass.

It is so firm and hard, and his general condition so good, that he will wait a month to see if it will not resolve spontaneously.

Though the doctor looks well and strong, and has gained in weight and strength, he has still a little fever every day.

The case was seen on June 30, 1894; guaiacol was used locally three times a day until September 1, when patient thought he was all right; during September and October patient was well; no pain; no enlargement noticeable.

All went well until the middle of November, when the place became a little tender again; there has been gradual enlargement with pain since: the swelling is now two-thirds as large as it was in June last: the temperature shows  $\frac{1}{2}^{\circ}$  to  $1\frac{1}{2}^{\circ}$  F. elevation each day.

This was by note to Dr. Osler, December 14, 1894. The last report from the patient was in June, 1895, when he states that the swelling has again subsided, leaving only a painless induration in its place.

Of six cases four occurred in men and two in women. In the reported cases the condition has been more frequent in men.

The ages ranged from twenty-one to forty-three years. Age is not believed to be a factor of any importance.

In a majority of cases the character of the typhoid fever attack bears no relation to the occurrence of these lesions. It was very difficult to obtain any correct account of the attack in most of these six cases.

The period after recovery from typhoid fever at which the lesions appeared varied from one to sixteen months. In two it was one month, in one two months, in another ten months, in another sixteen months, while in the remaining case the condition has not yet gone on to necrosis, but has recurred and subsided spontaneously now for the second time.

Sir James Paget described this condition as coming on when the patient was "well of his fever" when the temperature had already become normal, and convalescence was well established. I have been unable to find, with one exception, that of Ebermaier,<sup>1</sup>

<sup>1</sup> Deutsches Archiv für klinische Medicin, 44, 1888-89, p. 141.

an authentic case appearing during the course of the fever, though several have followed very early in convalescence. A large number of instances, however, of suppuration in the soft parts, either of typhoid or mixed infection, are on record, but the above case of Ebermaier's was a pure typhoid infection occurring on the thirteenth day of the fever. The latest instances range from between ten and a half and eighteen months after the subsidence of the fever.

As to the bone involved, hardly any region of the body is exempt. The tibia is undoubtedly the bone of choice, instances in this situation greatly predominating. The humerus, radius, ulna, femur, and fibula have at one time or another been involved, whereas the feet and hands are remarkably free, a case observed by Ebermaier being the only instance I can find. In the head, the parietal and temporal bones have been affected, and in the thorax the ribs or their costal cartilages are a very common seat, probably next in frequency to the tibia. The so-called typhoid spine, supposed to be an example of the same condition in the vertebral column, is probably a neurosis. As stated above, the rarity of cases in which the hands or feet were involved is quite striking. In this connection I might say that recently a patient came to the out-door clinic of this hospital, and in giving his history spoke of an attack of typhoid fever some eight or ten years previously. On his right hand a cicatrix was noticed on the dorsal surface between the third and fourth knuckles, and on being questioned regarding it, he gave the history of an inflammatory swelling which came on during convalescence from typhoid fever (two weeks after the fever had subsided), broke down, was opened, and healed after nine weeks' treatment. Possibly this is a case in point.

In the cases here reported the lesions were in three cases in the ribs or their costal cartilages, in one case in the tibia, in one both tibiae (only one being worked out bacteriologically), and in one the left radius and right tibia.

Usually the first symptom is pain. In three of our cases this was complained of while the patient was still in bed convalescing from his typhoid fever, in the others soon after being up and

about. The pain is usually localized, but in one of these cases was widely disseminated, shifting from one region to another. It almost invariably attacks the region subsequently the seat of the necrosis. The condition has been likened to the bone pains of secondary lues. This pain usually subsides after a short time, becoming almost unappreciable, or leaving but a slight soreness over its former seat. In the painful area a slight swelling may occur, also subsiding with the pain. The duration of the swelling varies; in some cases the trouble soon recurs with pain, swelling, and indications of necrosis; in others this may be delayed for months; while again in others there may be repeated exacerbations and subsidences, never going on to necrosis.

There is, as a rule, an entire absence of fever, and the clinical course is marked by a peculiar chronicity. The symptoms at the time of necrosis are all increased; the pain becomes more severe, the surface temperature is elevated, but there are no constitutional signs. On incision the pain is relieved, but a sinus may continue to discharge for months or years.

Chantemesse and Vidal speak of a case of periostitis of the tibia appearing during convalescence, which was treated by incision, the wound remaining open, and still discharging at the time of their reporting the case four years later. Sultan has observed a case of necrosis of the ribs discharging spontaneously, and persisting with sinus formation for six years.

Cases II and III are instances of what has been previously described by Chantemesse and Vidal.<sup>1</sup> In both the initial pain appeared shortly after recovery from typhoid fever, while the patient was up and about. This pain was accompanied by some thickening of the tissues in the painful part. Within a short time both pain and induration subsided, but not entirely, and there remained in Case II a noticeable induration with more or less tenderness, but no actual pain; while in Case III a definite rounded periosteal node persisted causing no inconvenience whatever. This condition lasted for fourteen and ten months respectively, at which times, from no apparent cause, a sudden exacerbation took place, both rapidly going on to necrosis. Chantemesse and

<sup>1</sup> Bull. et Mém. Soc. Méd. des Hôp. de Paris, Nov., 1893.

Widal speak of the condition appearing as a periosteal node or exostosis, or later as a periosteal abscess, which is precisely what occurred in Case III. These writers definitely separate these specific typhoid bone lesions from those due to mixed or pyogenic infection. They draw attention to the late period at which the onset follows the typhoid fever attack, to the subnormal temperature, and to the absence of septic signs, and refer to them as "suppurations froides," likening them to the exostoses of syphilis and the cold suppurations of tuberculosis.

There is a certain proportion of cases in which necrosis does not take place. These of course cannot be subjected to bacteriological study, but they are in every other particular so similar to the foregoing that they may be placed in the same category. Sir James Paget refers to one patient who remained subject to repeated attacks of pain and swelling of the periosteum three years, yet without any sign of suppuration or abiding change of structure beyond a slight thickening. Orloff has observed the same tendency of some cases to resolve. In one series of experimental inoculations<sup>1</sup> with typhoid bacilli, in a few instances resolution of a definite tumor was noticed, after having existed for quite long periods of time, whereas in others the tumor broke down.

Case VI is an instance in which the node resolved. The onset was, as in the other cases, during convalescence; later the tumor formed over the costal margin, but slowly subsided. Almost eight months "post-typhoid" it again appeared, and recently—about one year from the onset—the patient reports a second subsidence of the condition, with a painless induration remaining in the affected area.

It may be that some of the cases of "typhoid spine" described by Gibney<sup>2</sup> should be placed in this class. It has been considered to be a perispondylitis involving the periosteum and fibrous structures about the spinal segments. In many respects its clinical history and course are similar to that of the cases

<sup>1</sup> Dmochowski und Janowski, *Centralb. für Bacteriologie und Parasitenkunde*, Bd. xv, No. 7, 1894.

<sup>2</sup> Transactions of American Orthopædic Association, Sept., 1889, and Johns Hopkins Hospital Reports, Vol. iv.

under consideration, except that the pain is so much greater, but here, as in the resolving cases elsewhere, the bacteriological proof is also wanting.

A satisfactory explanation of the occurrence of bone lesions after typhoid fever has not as yet been advanced, but many valuable observations have been made.

The discovery by Quincke of the typhoid bacillus persisting in the bone-marrow after the attack presupposes a lowered vitality and susceptibility of the tissues so involved, but the setting up of a necrosis in one case and not in another is the point difficult to explain.

As to the influence of trauma allowing the presence of the typhoid bacillus in the bone-marrow and the resulting lowered vitality, trauma is doubtless in many cases an important factor. There are, however, many instances in which no such history can be obtained, and there are those showing multiple lesions, as that reported by Fürbringer, which can hardly come under this heading.

The effect of overstrain and muscular exertion, as brought out by Keen, is suggestive. He reports the case of a man who, some months after recovery from typhoid fever, returned to his occupation as rivetter in an iron works, which necessitated much standing and hammering, the strain thus falling mostly upon the right arm and leg. There shortly appeared a swelling of the right arm, and later formation of fistulous tracts through which pieces of dead bone came away. After recovery he returned to work, when a similar condition appeared in the right thigh and later in the left. The interesting point is that the lesion of the arm was at or about the deltoid insertion, and that of the right thigh at the insertion of the glutæus maximus, and that of the left at the lesser trochanter, all these being points upon which strain would fall in such acts as standing and hammering.

In the cases of typhoid spine reported by Gibney, a definite history of injury was given in two, but in many others no such history can be obtained. Of the fourteen cases reported by Chantemesse and Widal, three showed a predisposing cause in an old fracture callus. Case IV was treated in Ward C of this hos-

pital during the attack, and while lying quietly in bed he experienced the first pains in the tibia. Subsequently he walked excessively, which may have favored the development of necrosis, but he had made no exertion, nor had there been a trauma before the first appearance of pain.

From the bacteriological notes of the cases here reported it will be seen that in four out of the five the typhoid bacillus was obtained in pure culture. The remaining case being a mixed infection, the lesion of the radius showed typhoid bacillus associated with the staphylococcus pyogenes citreus, and the tibia, the staphylococcus pyogenes aureus alone. The wound of the tibia in this case had been opened, and therefore exposed to contamination from without for about ten days previous to the time of taking cultures, but this would not, so far as we know, have resulted in causing the disappearance of the typhoid bacillus had it ever been present. The length of time that these sinuses may remain open and exposed to external contamination, and yet be proof against it, is very remarkable. In Case I, at time of admission, the sinus had been discharging for three months, yet cultures from it showed the typhoid organisms alone. In Case IV the exposure was but for a few days, yet it was free from contamination. The most striking example of this, however, is the case reported by Sultan, in which the wound remained open for six years, yet at the end of that time cultures from the open sinus showed the typhoid bacillus unassociated with any other organism. Others have noticed the persistence of the typhoid bacillus in the wound alone, or associated with other organisms, in a large number of instances. Chantemesse and Vidal observed one case of six months', and another of four years' duration, and D. Buschke has reported a case of abscess of a rib showing the organisms seven years after the attack.

Cases I, II, III, and IV all showed typhoid bacillus in large numbers before operation. In Cases I and II, the lesion being situated in the chest-wall, and infiltrating deeply into it, all the diseased tissues could not be removed. After the operation the organisms were still found in the wound, which showed little tendency to heal beyond a certain point. Extensive secondary

operations were accordingly performed, and yet cultures three and a half months later showed the organism in one of the cases. The necrosis again had deeply infiltrated the thoracic wall. Recovery in these cases was slow.

In Cases III and IV the lesion was situated in the tibia, and in each case an extensive operation was performed, removing all diseased and suspected tissues, both in bone and soft parts. In Case IV cultures were taken at the first dressing on the ninth day, which proved to be negative. In both of these cases recovery was rapid and uninterrupted, the patients being discharged from hospital—wounds healed—on the twenty-seventh and twenty-first days respectively.

There can be little doubt that the chronicity of the process, and the long periods that the sinuses continue to discharge, are due to the persistence of the organism in the focus. The study of these four cases, though a small number, suggests this very strongly, and points to the fact that complete removal of the diseased tissues alone may be followed by rapid and satisfactory results.

The bacteriological technique in the working out of these cases was as uniform as possible. In three of the five cases the pus was plated in agar almost immediately, and in the other cases the agar slants taken at the time of operation showed the separate colonies so discretely that they served the same purpose.

In all cases cover-slips from the pus were examined, but in one case only were the organisms found. This difficulty of staining typhoid bacilli in cover-slip appears to have been the experience of many, the explanation lying in the fact that in the first place, they stain very poorly, and in the second, that they very readily part with that stain when subjected to decolorizing agents.

The growth on nutrient agar-agar and gelatin, potato, and sugar agar, in bouillon and litmus milk, and the reaction when subjected to the test for indol, were all characteristic of the typhoid bacillus.

In Case V, in some instances a growth was seen upon potato, but subsequent implantations resulted in the usual invis-



ble multiplication of the organism as proved by cover-slip preparations. This visible growth has frequently been met with, but does not disprove the identity of the bacillus as it is considered to arise from some peculiarity in the culture medium.

The test with metallic mercury, as described by Dr. Bolton,<sup>1</sup> showed the double zone characteristic of the typhoid organism in all the instances in which it was applied.

Morphologically, the organism was a short bacillus with rounded ends, freely segmenting, and forming at times long chains. In addition were larger bacilli with ends more square, seen singly, in pairs, and forming long threads. These latter forms were very constant. Nothing resembling spores was seen.

Motility was marked, especially in the smaller forms; in the larger less so. The long threads moved by slow, wavy motion across the field of the microscope.

As to the staphylococcus pyogenes citreus and aureus, conclusive descriptions of the cultural reactions obtained are given with the cases in which these organisms occurred.

In the study of these cases the bacteriological considerations are of course the more important, and the pathological considerations are usually dismissed with a few words. The character of the lesion has, however, of late given rise to much speculation with some who would seek to prove it a necrosis rather than a true abscess formation. This has been based largely upon the appearance of the pus, and the microscopical examination of the same. In an article Klemm<sup>2</sup> speaks of this, and definitely states that a difference exists between the lesion produced by the local typhoid infection and that of the pyogenic cocci. The exudate in the typhoid infections he describes as being rich in detritus and containing but a comparatively small number of leucocytes, and he states that it should not be called pus.

The chronicity of the process, so frequently seen, has caused it to be considered by some analogous to the cold suppurations of tuberculosis, and the necrosis of syphilis; in fact, it has been

<sup>1</sup> International Medical Magazine, December, 1894.

<sup>2</sup> Archiv für klinische Chirurgie, Bd. XLVII.

classed with the infectious granulomata. So far, however, nothing has been found in the diseased tissues which can be considered characteristic of, or peculiar to, this condition. A small cell infiltration with a greater or less leucocytic infiltration has been seen in all, the development of new tissue varying with the length of time the disease has existed. In some of the more acute, the infiltration is intense, and in one case we have observed a rather diffuse necrosis, as we thought from the gross appearances, but on microscopic examination it was found that nuclear staining was still present, though very faint. In this case (No. IV) the appearances at the time of operation were quite striking. The case was the most acute that we have seen, and came on at the shortest period after the primary disease, and was operated upon six days after necrosis was established. The focus of necrosis was quite circumscribed over the crest of the tibia, but the tissues surrounding it were of a grayish translucent appearance, strongly suggested a condition of necrosis. This, however, as before mentioned, showed faint nuclear staining.

As to the pus obtained from these cases, it is difficult to say that there was any characteristic feature. In Cases I and III the pus was of a brownish-red color, very thick, and gelatinous and odorless. In Case IV it was grayish in color, thick but not tenacious, and also odorless. Whereas in Case V (tibia), which showed the staphylococcus aureus alone, the pus was apparently identical with that of I and III, which were purely typhoid cases, in that it was of the same color and equally thick and gelatinous. Examination of the pus showed rods in Case II alone. In two of the cases there appeared to be an abundance of detritus present and a noticeably small number of pus cells, many of which showed considerable fragmentation. The gross appearance of all the cases was decidedly ragged and necrotic, though the same must also be said of the tibia in Case V, which was a purely aureus infection.

The *diagnosis* of these cases would rest largely upon the history of a previous typhoid fever, or perhaps some indefinite continuous fever. In Case V the diagnosis of typhoid fever was made only by the examination of the pus from the radius some

weeks after the febrile attack had subsided. The occurrence during or after convalescence is suggestive of the purely typhoid cases, particularly in bone, whereas the mixed infections in bone and soft parts, and the typhoid infections in the soft parts are seen more frequently during the course of the disease.

The *prognosis* is good, as a rule, although in the article just referred to, Klemm reports a fatal case of disease of the femur showing typhoid and colon bacilli associated.

Complete excision of all diseased and suspected tissues appears to be the most satisfactory treatment. In the earlier writings this point was brought out, and mere incision was denounced as being insufficient. The persistence of the organism in the wound for such long periods of time, as some cases show, and the satisfactory results obtained after thorough and complete removal of the focus, suggest very strongly the lines along which to work.